C-G C-G G-C•

AUAAACUAAGGAAUaucuaug . uaauauau CAA

SEQ. I.D. NO. 345

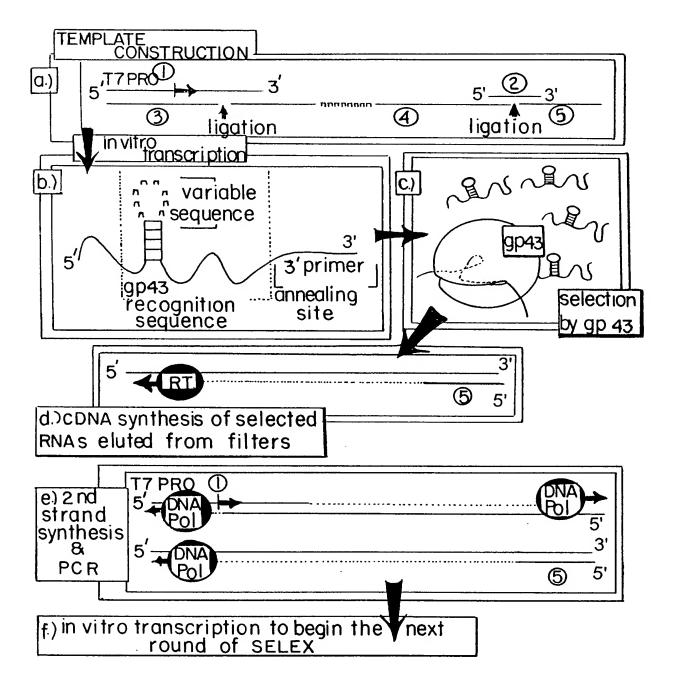
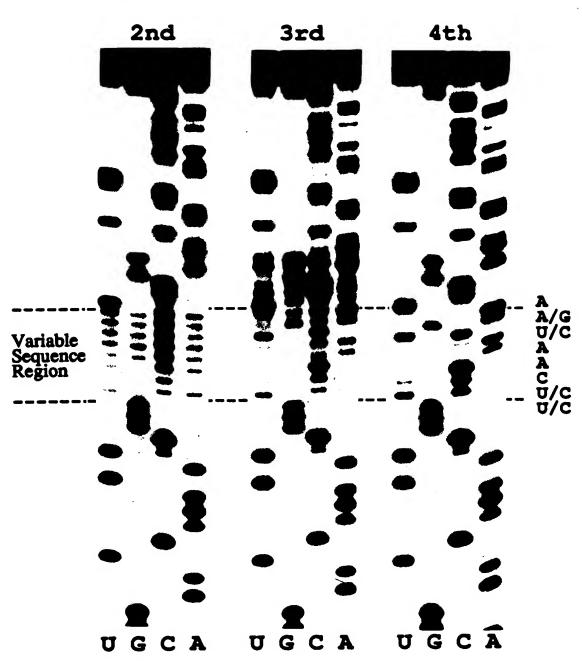


FIG.2

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Express Mail No. EL652339952US

FIG. 3

## SELECTION CYCLE:

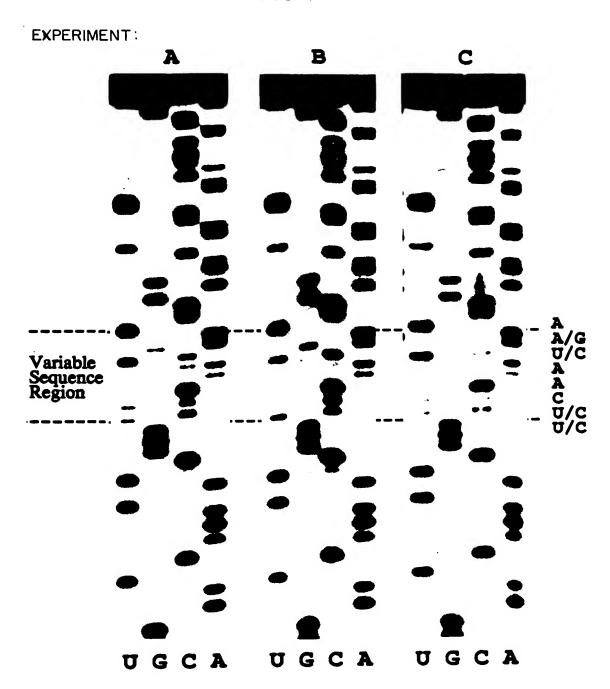


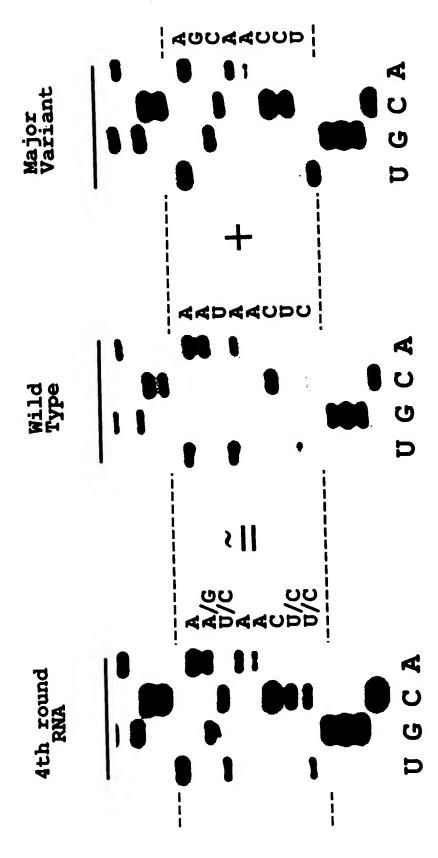
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Inventor: Gold et al.

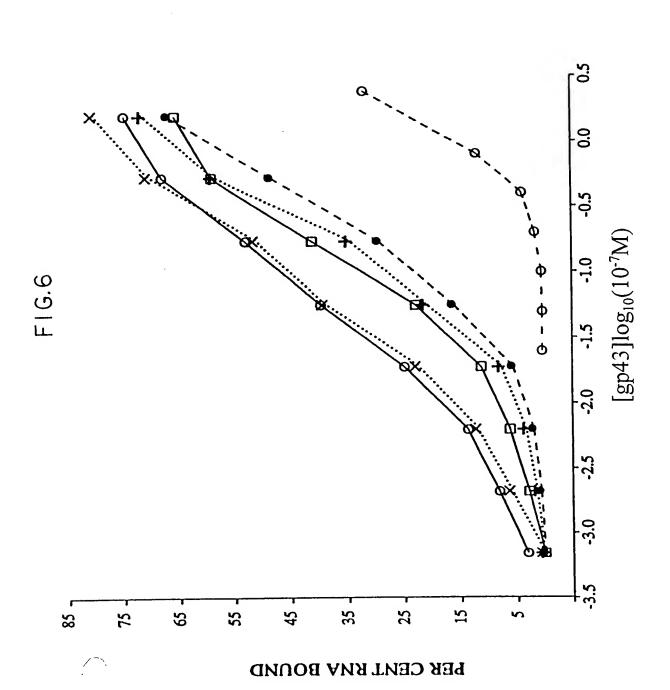
Express Mail No. EL652339952US

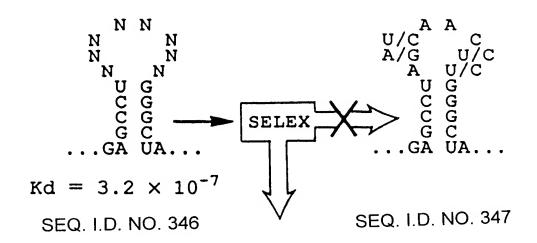
FIG.4





F16.5





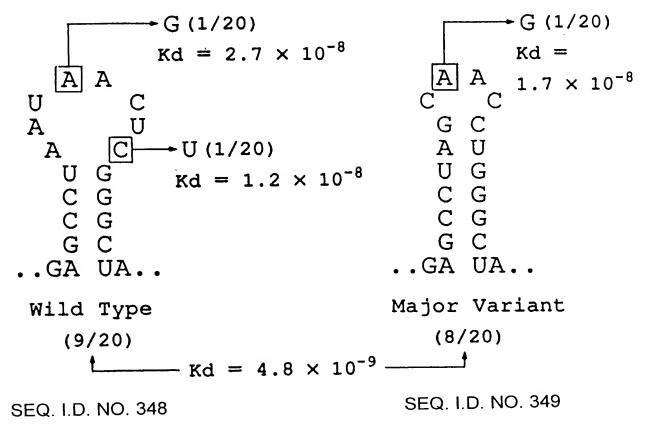


FIG.7

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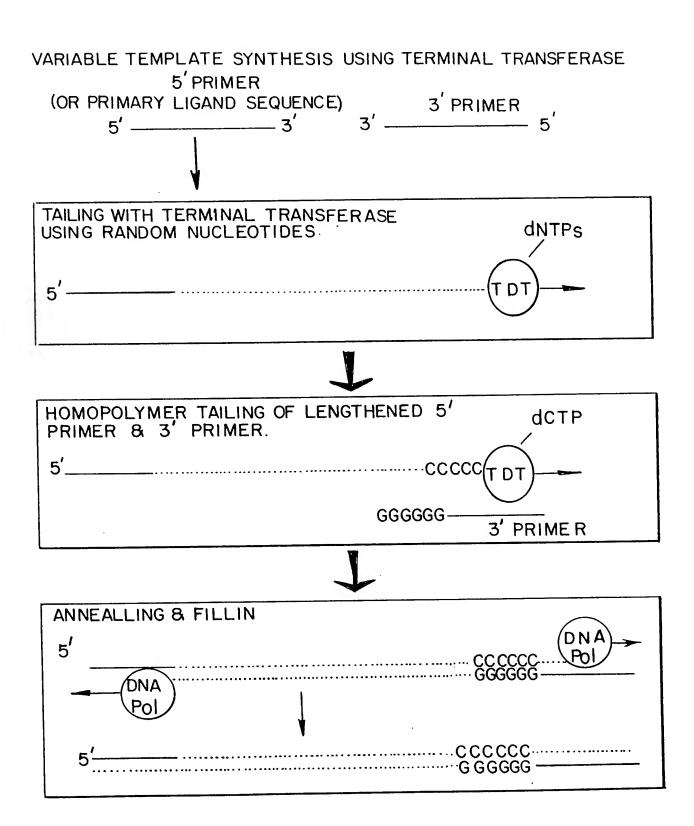


FIG.8

"WALKING" BY EXTENDING THE PRIMARY LIGAND. **SECONDARY** BINDING SITE ASYMMETRIC PCR YIELDING SINGLE-STRANDED COPIES OF **EVOLVED** PRIMARY PLUS STRAND PROTEIN OF LIGAND INTEREST VARIABLE TEMPLATE SYNTHESIS USING TERMINAL TRANSFERASE 5' PLUS STRAND -CCC CCC ĞĞĞĞĞĞ FURTHER SELEX TO ISOLATE HIGHER AFFINITY LIGANDS **SECONDARY** LIGAND INTERACTION PRIMARY LIGAND PROTEIN OF INTERACTION INTEREST

FIG.9



## ANCHORING OF BRIDGING OLIGONUCLEOTIDE & SECONDARY LIGAND EVOLUTION.

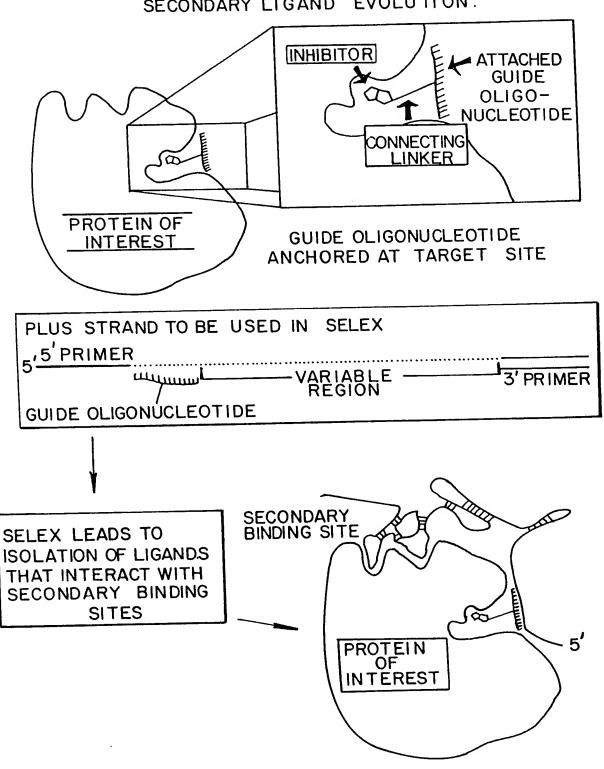


FIG.10

LOBIE GAEZEOUI

SECONDARY LIGAND-DIRECTED PRIMARY LIGAND EVOLUTION .

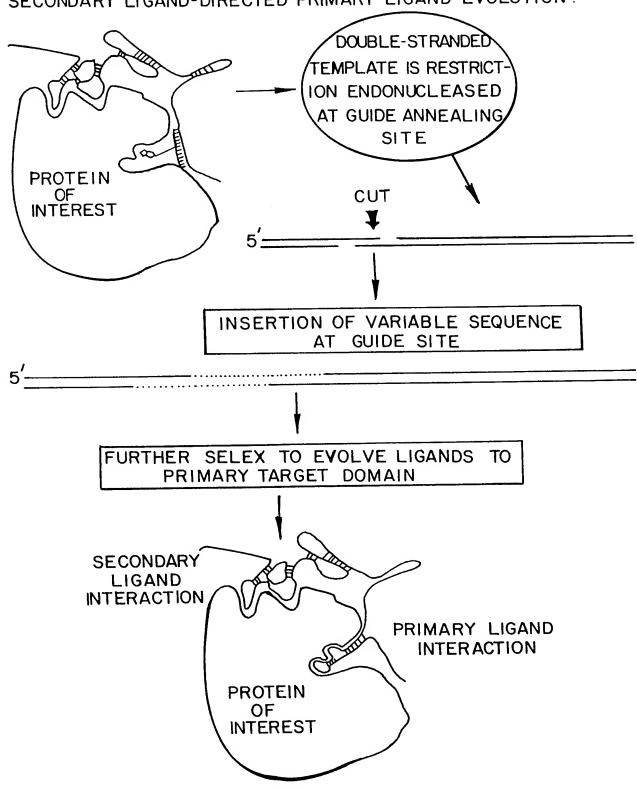


FIG.11

Sheet 12/34 Express Mail No. EL652339952US

3'-gttagttc 3'-attatgctgagtgatatccctcgtagtctgaaaattagact-5' ligation

SEQ. I.D. NO. 351

5'-taatacgactcactatagggagcatcagacttttaatctgacaatcaag-.

SEQ. I.D. NO. 350

promoter

LT

in vitro transcript

-gggagcaucagacuuuuaaucugacaaucaag[32n]aucuaugaaagaauu 2,

F16.12A

FIG. 12 B

→ I2A

5'-atctatgaaagaattttatatctc-3'

3'-cttaaaatatagagataactttgcctaggcc-5'

ligation

SEQ. I.D. NO. 352

1

32n..tagatacttt-5'

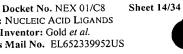
SEQ. I.D. NO. 353

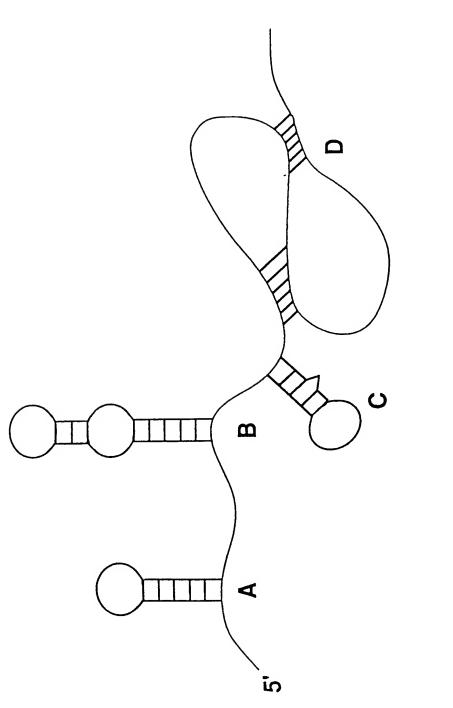
unauaucucuauugaaacggauccgg-3'

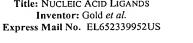
← 12A

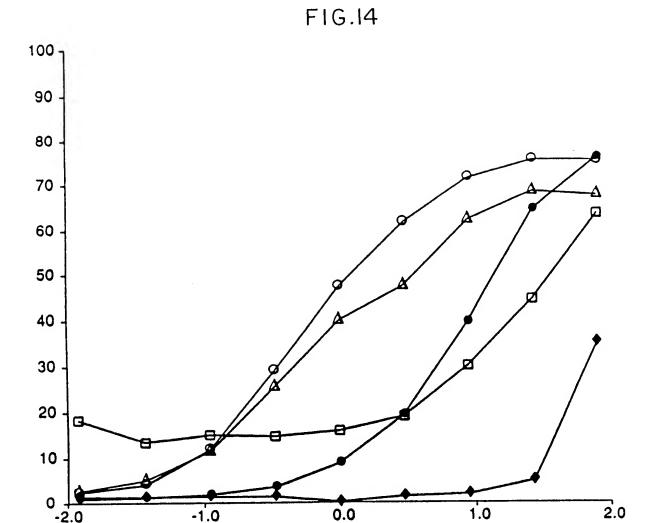
SEQ. I.D. NO. 354

F16.12B









Δ I.I ucaagAAUUCCGUUUUCAGUCGGGAAAAACUGAACA aucu (13)

[HIV-RT] log<sub>10</sub>(nM)

- O 1.3 UCAGAAUAUCUUCCGAAGCCGAACCGGAAAACCGGCAUCU (1)
- ☐ 1.4 ucaagggcaucugggaggguaaggguaagguugucggaucu (4)

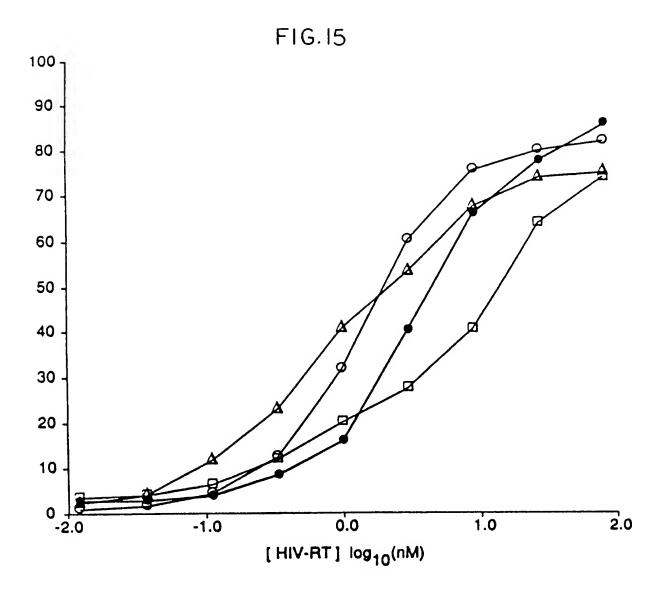
 $\triangle$  1.1 = SEQ. I.D. NO. 355

● 1.3 = SEQ. I.D. NO. 357

O 1.3 = SEQ. I.D. NO. 356

☐ 1.4 = SEQ. I.D. NO. 358





ISOLATE
 ○ 2.1 a ucaag -- AAUAUA - UCCGAACÜCGACGGGAUAACGÁGAA-Gaucu (3)
 □ 2.2 b ucaaguaccuaggauaaaaagggagaacácacguguga - cu (13)
 • 2.5 b ucaagacaguauccguucuugaùcaucgggacaaaugáaucu (3)
 △ 1.1 ucaagaauuccguuùucagucgggaaaaaácúgáacaaucu (13)

O 2.1a = SEQ. I.D. NO. 359

● 2.5b = SEQ. I.D. NO. 361

 $\Box$  2.2b = SEQ. I.D. NO. 360

 $\triangle$  1.1 = SEQ. I.D. NO. 362

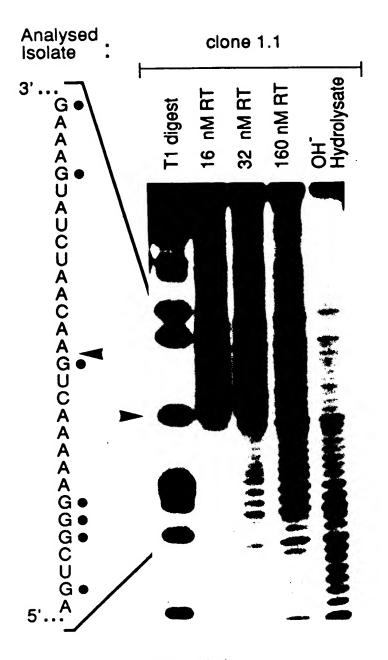
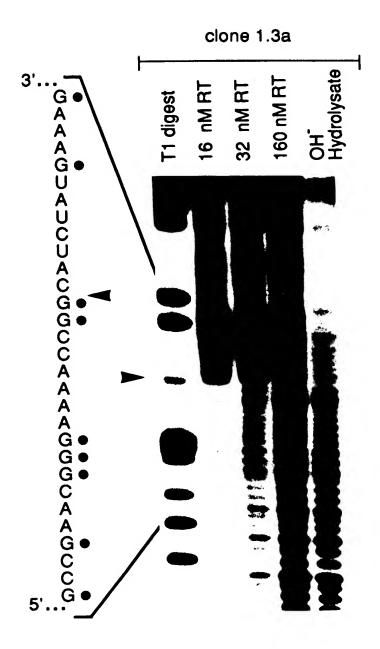


FIG. 16 A

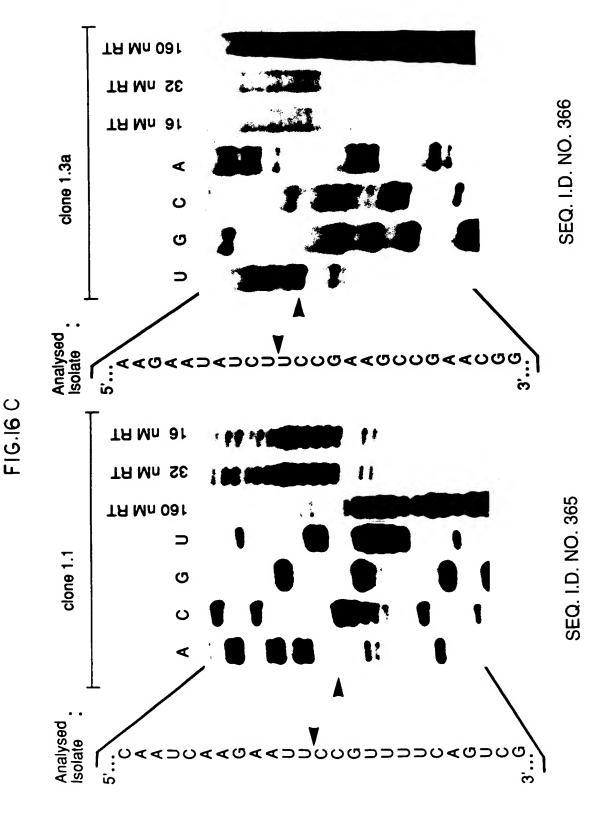
SEQ. I.D. NO. 363

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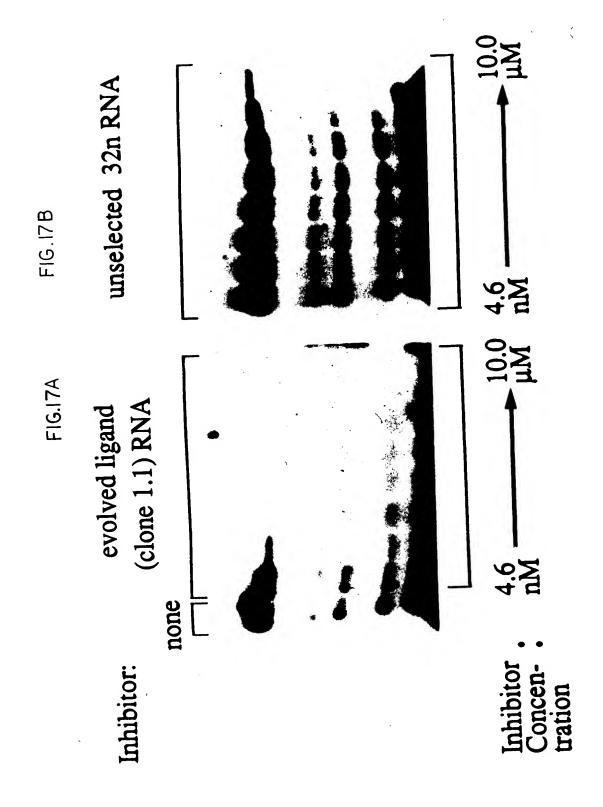
F1G.16 B

SEQ. I.D. NO. 364

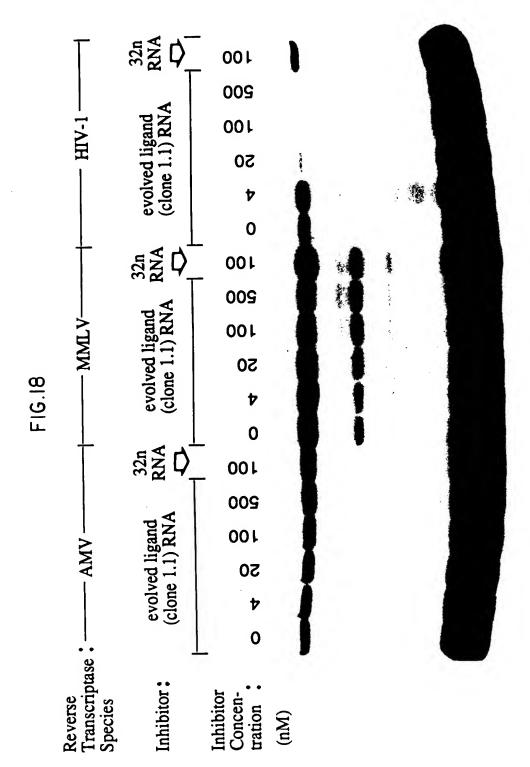


\*\* = . ;

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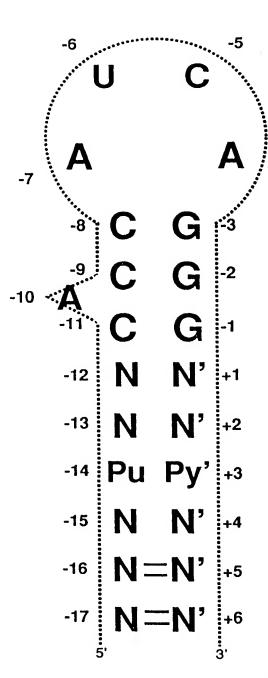


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Express Mail No. EL652339952US



Express Mail No. EL652339952US

FIG.19B



	Α	С	G	U
-4	36	0	0	0
-5	0	36	0	0
-6	4	3	1	28
-7	36	0	0	0
-10	36	0	0	0

	AU	CG	UA	GC	UG	GU	Bulge	END
-8/-3	0	24	0	12	0	0	0	0
-9/-2	0	25	0	10	1	0	36	0 .
-11/-1	0	24	2	10	0	0		4
-12/+1	8	1	8	10	7	1	0	
-13/+2	6	5	8	9	3	1	3	3
-14/+3	9	0	4	10	2	3	3	4
-15/+4	4	0	9	6	0	1	6	8
		1		1	1	3	0	2
-16/+5	10	<del>  `</del>	2	1	┼		1	1
-17/+6	0	4	6	1	4	2		<u> </u>

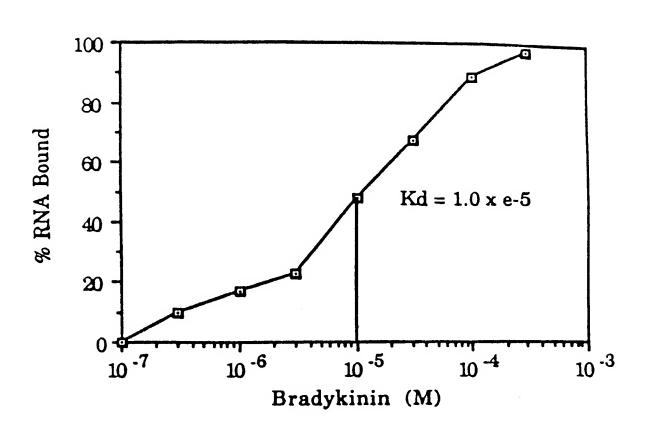
FIG.19C

FIG.19A

SEQ. I.D. NO. 367

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Express Mail No. EL652339952US

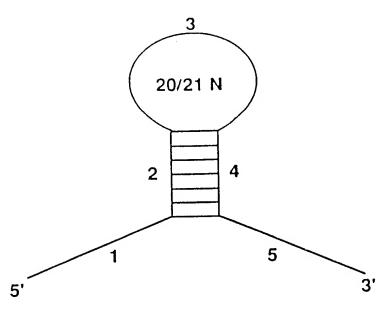




10037985 101801



FIG.21A



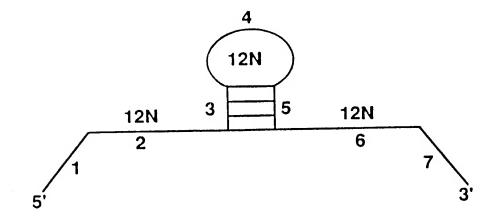
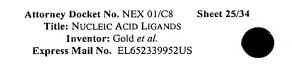
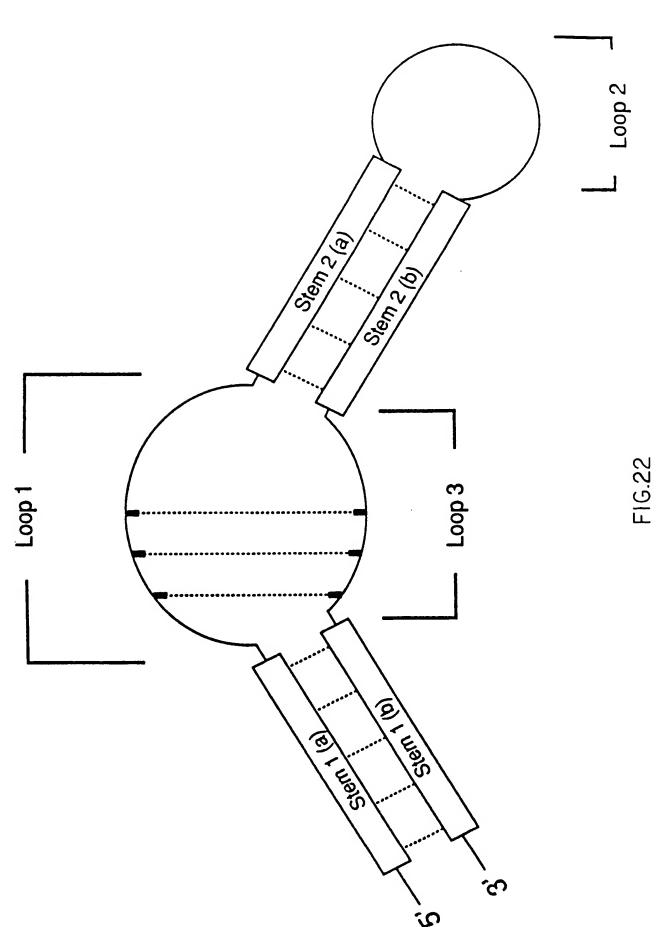


FIG. 21B





## FOOMYGOOM ... HOLLEDIA

Motif I (6a)

CAC U (NUCLEOTIDES 2-38 OF SEQ. I.D. NO. 301) GUG U UUGAGAAA 5'...gGGUGCA3'...ucuaUGU

Motif II (1c)

Motif III (9a)

ugaa-3' GCUU-5' CC UUGaucua-A GG

SEQ. I.D. NO. 369

SEQ. I.D. NO. 368

WT (Motif II-like Domain)

U ACGGUA
A GACGCUG || CA...
CUGCGAC || GU...

SEQ. I.D. NO. 370

F16.23

K CAGC

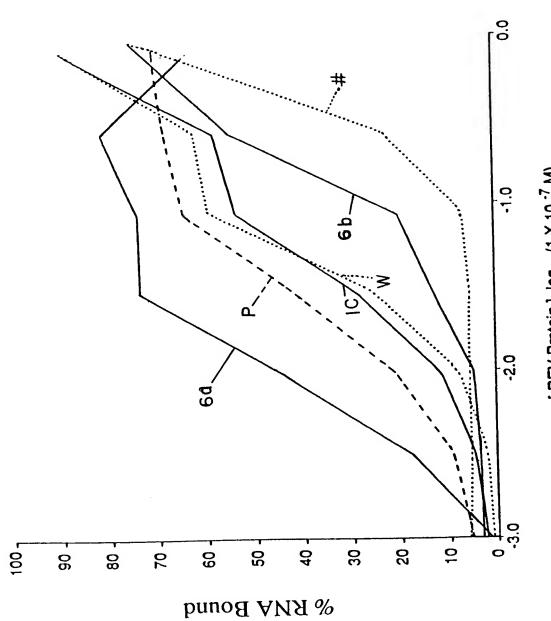
UCU

AAGAUA

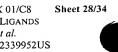
5'...AGAUG
3'...ucuAC

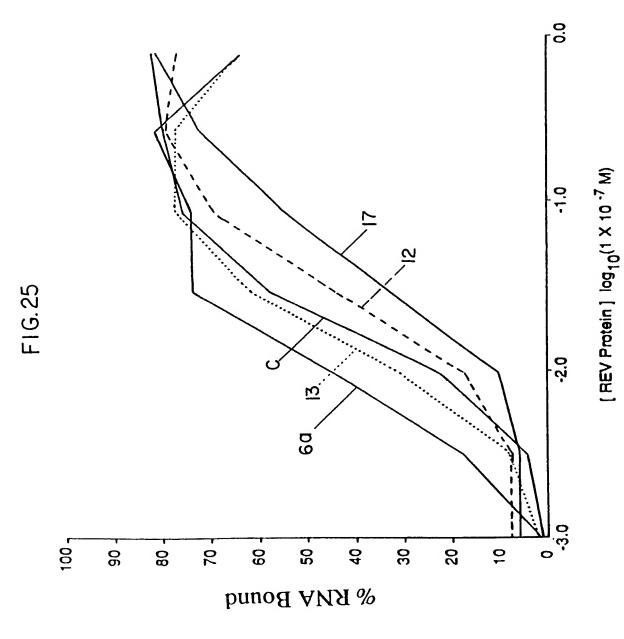
-ACA-G

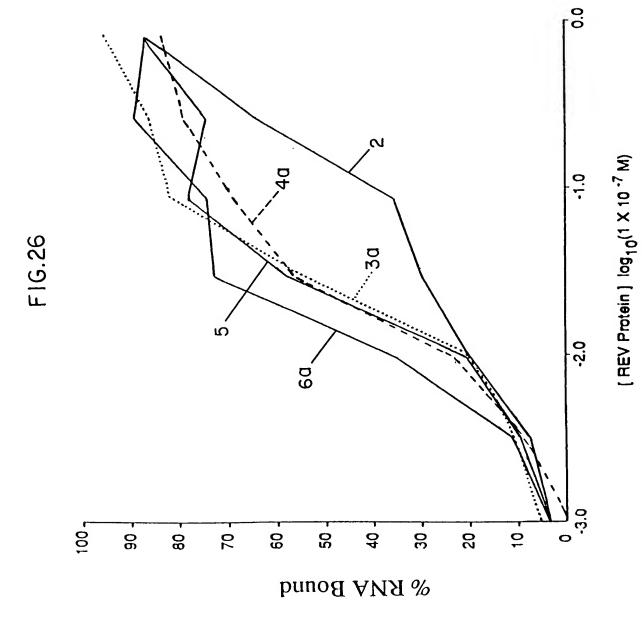
16.24

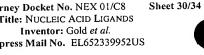


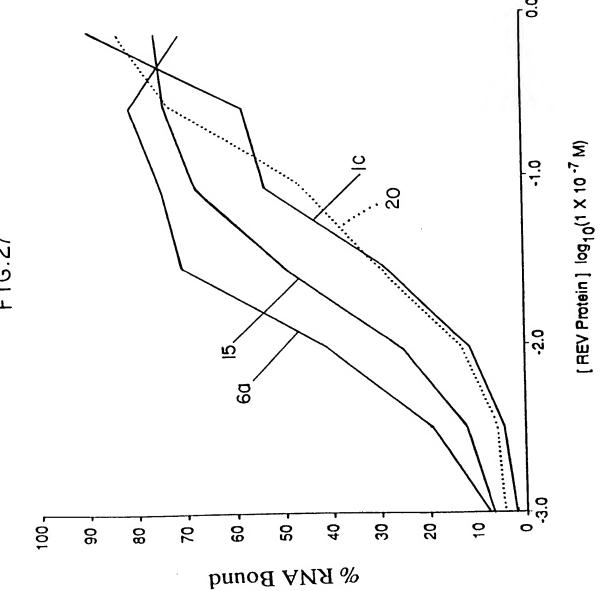
[ REV Protein ]  $\log_{10}(1 \times 10^{-7} \text{ M})$ 

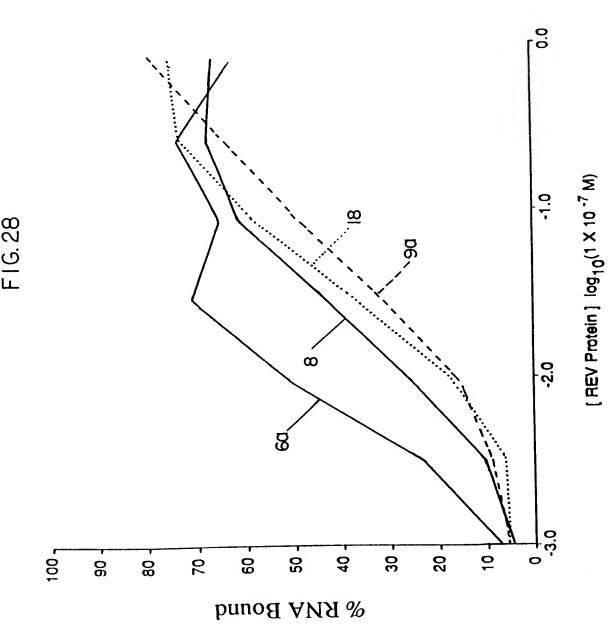






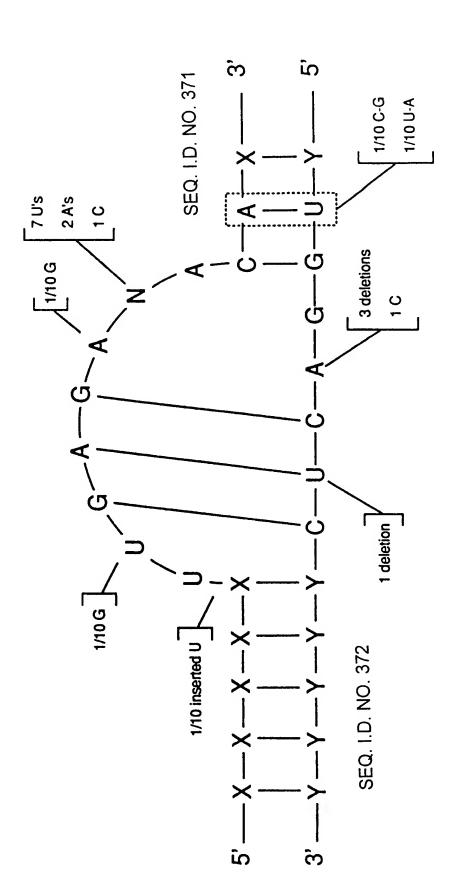


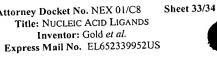


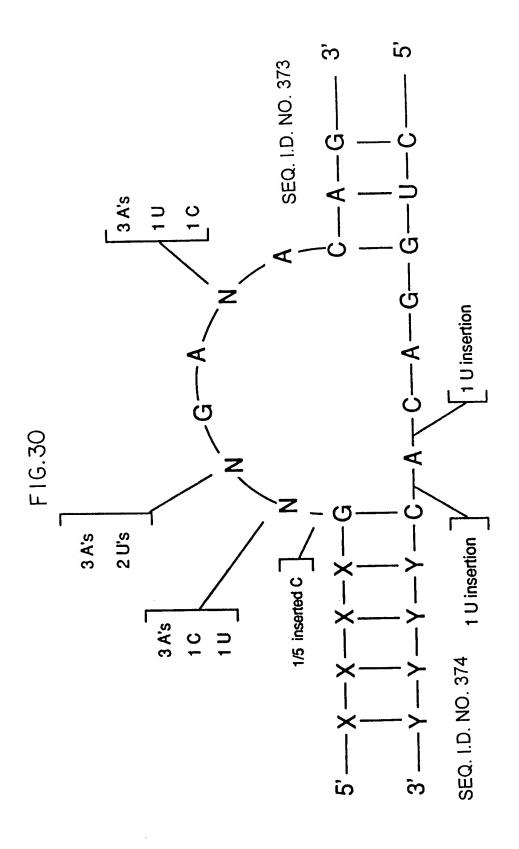




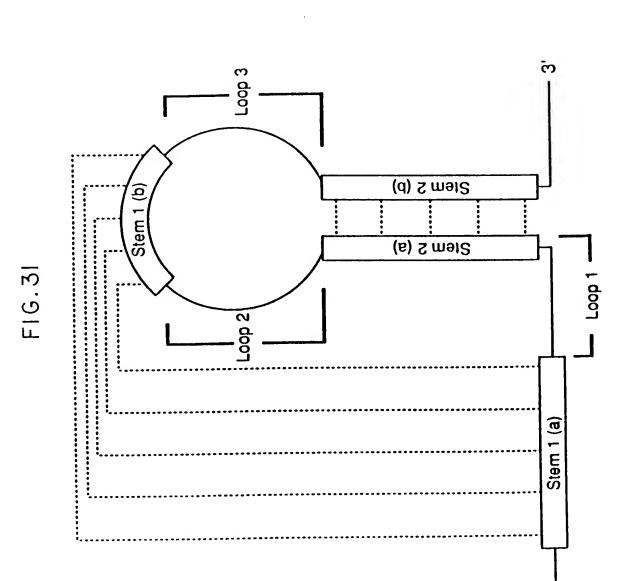
TOOSYSE TOISOI







d.



က်